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PII: S0040-4020(16)30879-1

DOI: 10.1016/j.tet.2016.08.084

Reference: TET 28065

To appear in: *Tetrahedron*

Received Date: 23 April 2016

Revised Date: 29 August 2016

Accepted Date: 30 August 2016

Please cite this article as: Dutta L, Sharma M, Bhuyan PJ, Regioisomeric synthesis of dihydrofuro[2,3-*d*]pyrimidines in a diastereoselective manner involving nitrogen ylides in one-pot three-component reaction, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.08.084.

Graphical Abstract

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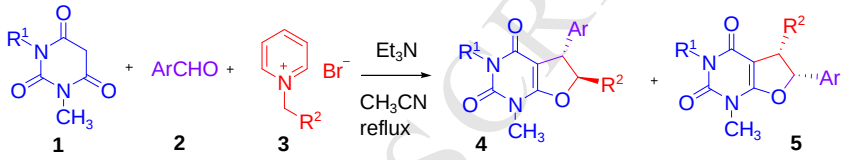

Tetrahedron
journal homepage: www.elsevier.com

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Pyrimidine,
Furo[2,3-*d*]pyrimidines,
Aldehyde,
Pyridinium bromide
Pyridinium ylide

ABSTRACT

Synthesized some novel regioisomers of furo[2,3-*d*]pyrimidines in a diastereoselective manner *via* one-pot three-component reaction of barbituric acids, aryl aldehydes and pyridinium bromides in the presence of triethylamine as base. Both the isomers were obtained in comparable ratio with excellent overall yield.

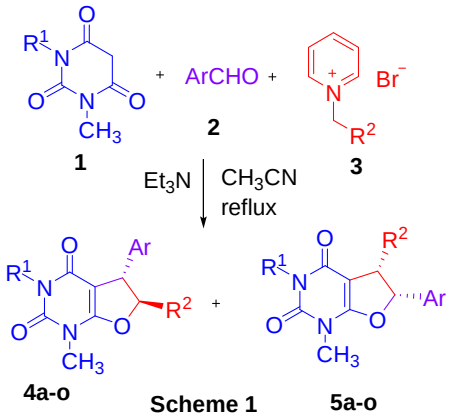
1. Introduction

Furopyrimidines, particularly furo[2,3-*d*]pyrimidines represent a very important class of compounds that possess wide range of biological activities such as antibacterial,[1] antifungal,[2] antitumor,[3] antiviral,[4] antifolate[5] and anti-human cytomegalovirus activity.[6] Compounds with this molecular motif are also active on blood circulatory system[7] and stimulate the skin preparative regeneration.[8] In view of the vast biological activities and importance to pharmaceutical discovery research, considerable attention has been diverted towards the synthesis and molecular manipulation of furo[2,3-*d*]pyrimidines. Furo[2,3-*d*]pyrimidines are usually prepared either from suitably functionalized furan ring[9] by generating the pyrimidine ring on the parent furan ring or from a pyrimidine derivative by constructing a furan ring on the parent pyrimidine ring.[10] Very recently, an excellent review was published describing various synthetic routes for furopyrimidines, particularly furo[2,3-*d*]pyrimidines.[11]

Nitrogen ylides represent an important class of nucleophilic or bifunctional reagents which can undergo cyclization, olefination, rearrangement reactions etc, and hence have wide application for the construction of diverse carbocyclic and heterocyclic compounds of synthetic and biological significance.[12] In this regard, pyridinium ylides have extensive application for the synthesis of dihydrofuran and its annelated derivatives which produced the desired compounds in a diastereosective manner.[13]

In continuation of our work on pyrimidines,[14] in the present paper, we report an unprecedented regioisomeric synthesis of some highly functionalized dihydrofuro[2,3-*d*]pyrimidines **4** and **5** in diastereoselective manner from one-pot three-components reaction of barbituric acids **1**, aryl aldehydes **2** and pyridinium bromides **3** in the presence of triethylamine as base (Scheme 1). During the reaction, nitrogen ylides were formed and involved in [4+1] annulation as well as [2+1] annulation processes which after intramolecular ring transformation produced the two regioisomeric products.

Synthesis of dihydrofuro[2,3-*d*]pyrimidines 4 and 5



Scheme 1

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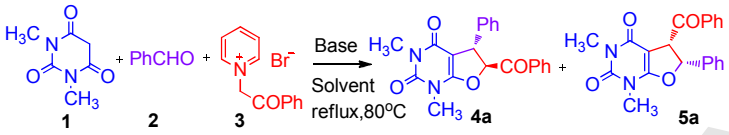
2. Results and Discussion

The study was initiated by performing the three-component reaction of *N,N*-dimethylbarbituric acid **1** (R^1 = Me), benzaldehyde **2** (Ar = Ph) and benzylpyridinium bromide **3** (R^2 = COPh) in various solvents and base to determine the optimal condition for the model reaction. Among the solvents *viz* water, ethanol, DMSO, dichloromethane and acetonitrile, the acetonitrile was found to be most effective. The reaction did not proceed in water as barbituric acid derivative **1** (R^1 = Me) was not soluble in the solvent. The model reaction was also investigated employing different bases *viz.* Et_3N, DBU and K_2CO_3. The results were summarized in Table 1. It was found that the reaction in acetonitrile and use of 1.2 mmol of Et_3N as base furnished the maximum yield of the two products **4a** and **5a** in less time duration in comparison to others (Entry 6). Therefore, all subsequent reactions were carried out under this reaction condition only. While, equimolar amount of the base is required just for the formation of the ylide from pyridinium salt, we observed that, the reaction proceeded in the presence of equimolar amount of the base providing very low yield of the products (Entry 5), and that indicated simultaneous formation of the ylide and the products in the reaction process.

Table 1[a]: Optimisation of solvent and base

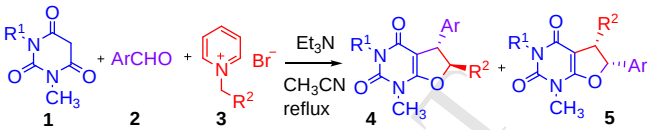


Entry	Solvent	Base (1.20 mmol)	Time (h)	Product	Yield%***
1	Water	Et_3N	10	**NR**	0
2	DMSO	Et_3N	7	**4a**	22
				5a	18
3	C_2H_5OH	Et_3N	8	**4a**	14
				5a	12
4	CH_2Cl_2	Et_3N	5	**4a**	13
				5a	11
5	CH_3CN	Et_3N*	4	**4a**	12
				5a	10
6	CH_3CN	Et_3N	4	**4a**	40
				5a	38
7	CH_3CN	Et_3N**	4	**4a**	36
				5a	33
8	CH_3CN	K_2CO_3	10	**4a**	15
				5a	12
9	CH_3CN	DBU	8	**4a**	23
				5a	19

[a]Reaction conditions: *N,N*-dimethyl barbituric acid (1mmol), benzaldehyde **(**1mmol), benzyl pyridinium bromide (1mmol) *1 mmol; **1.5 mmol; *** isolated yield

Increase in the load of the catalyst beyond 1.2 mmol did not improve the yield of the products (Entry 7). The model reaction was initiated with the preparation of benzylpyridinium bromide **3** (R^2 = COPh) from the reaction of phenacyl bromide and pyridine in ethyl acetate at room temperature following the existing reaction procedure.[15]

Table 2[a]: Synthesis of dihydrofuro[2,3-*d*]pyrimidines 4 and 5



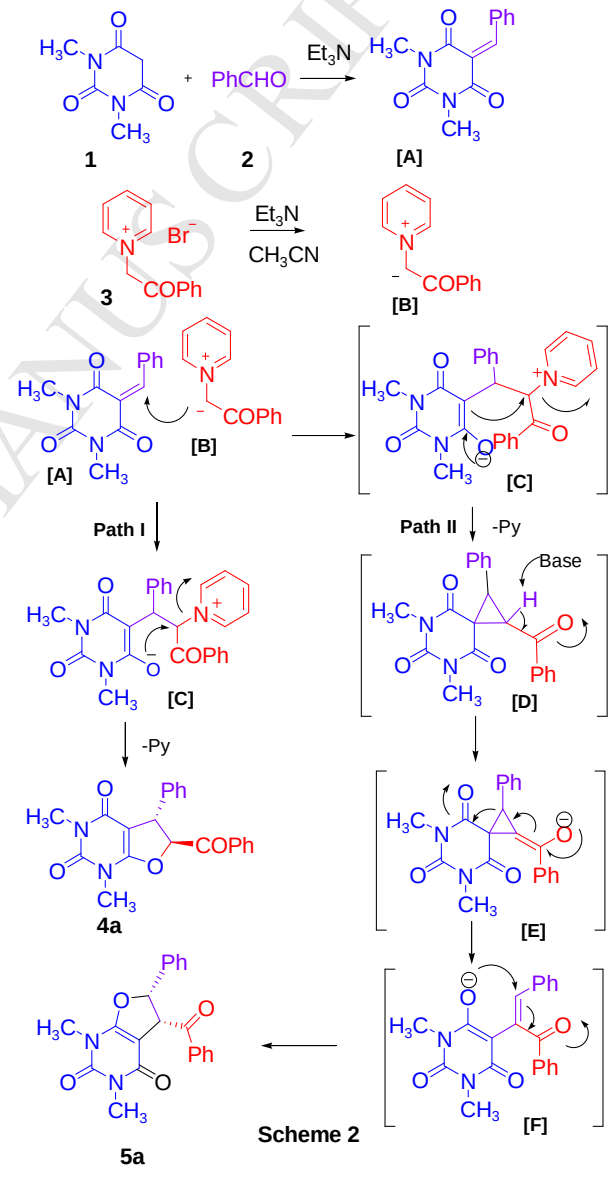
Ent.	R^1	Ar	R^2	Prod.	Time (h)	Yield[b] %
1	CH_3	C_6H_5	COPh	**4a**	4	40
				5a		38
2	CH_3	*p*-CH_3-C_6H_4	COPh	**4b**	4.5	36
				5b		33
3	CH_3	*p*-NO_2-C_6H_4	COPh	**4c**	2.5	45
				5c		42
4	CH_3	*p*-Cl-C_6H_4	COPh	**4d**	3.5	43
				5d		40
5	CH_3	*p*-Br-C_6H_4	COPh	**4e**	3.5	42
				5e		40
6	H	C_6H_5	COPh	**4f**	5	35
				5f		32
7	CH_3	C_6H_5	COOEt	**4g**	5	40
				5g		36
8	CH_3	*p*-OCH_3-C_6H_4	COOEt	**4h**	6	32
				5h		28
9	CH_3	*p*-CH_3-C_6H_4	COOEt	**4i**	6	36
				5i		34
10	CH_3	*p*-NO_2-C_6H_4	COOEt	**4j**	3h	44
				5j		40
11	CH_3	*p*-Cl-C_6H_4	COOEt	**4k**	4	42
				5k		39
12	CH_3	*p*-Br-C_6H_4	COOEt	**4l**	4.5	41
				5l		39
13	H	C_6H_5	COOEt	**4m**	6	33
				5m		30
14	CH_3	C_6H_5	CN	**4n**	3.5	37
				5n		34
15	CH_3	*p*-Cl-C_6H_4	CN	**4o**	3	38
				5o		35

Ent. = Entry, Prod. = Product,
[a]Reaction conditions: Substituted Barbituric acid **1** (1mmol), Aryl aldehyde **2** (1mmol), Pyridinium ylide **3** (1mmol), Et_3N (1.20 mmol), CH_3CN (5ml), [b]isolated yield

The benzylpyridinium bromide **3** (R^2 = COPh) so obtained was treated with *N*,*N*-dimethylbarbituric acid **1** (R^1 = Me) and benzaldehyde **2** (Ar = Ph) in one-pot three-component reaction protocol in refluxing acetonitrle in the presence of triethylamine as base. The progress of the reaction was monitored by TLC which indicated the formation of two products. The reaction was allowed to reflux for 4 hours till the completion of the reaction. The solvent was removed under reduced pressure and the compounds were separated by chromatographic methods and isolated the expected dihydrofuro[2,3-*d*]pyrimidines **4a** (Ar = Ph, R^2 = COPh) along with unexpected regeoisomeric compound **5a** (Ar = Ph, R^2 = COPh) in 40% & 38 % yield respectively in a diastereoselective manner. The generality of the reaction was established by synthesizing the compounds **4a-o** and **5a-o** by utilizing various substituted barbituric acids **1**, aryl aldehydes **2** and pyridinium salts **3** and characterizing them (Table 2). The structures of the compounds were ascertained from the spectroscopic data and elemental analysis. As for example, in the ^{1}H NMR spectra, the two protons at 2,3-positions of dihydrofuran ring of compound **4a** (Entry 1) display two doublets at δ 4.04 and 4.19 with the vicinal coupling constant J = 9.5 Hz. It is well recognized that stereochemical relations among vicinal protons in fused dihydrofurans cannot be reliably determined by simply measuring coupling constants *e.g.* changing the size of the substituent at the dihydrofuran ring of benzodihydrofurans causes a reversal in the value of J_{cis} and J_{trans}.[16] In view of that, the NOESY NMR spectra of the compound was studied properly where the two protons showed no corelation, and hence it was concluded that the product **4a** was *trans* dihydrofuro[2,3-*d*]pyrimidines. In contrary, ^{1}H NMR spectra of the other compound (Entry 1) showed two protons of the dihydrofuran ring as two doublets at δ 5.16 (J = 5.5) and 6.04 (J = 5.5) ppm respectively which indicates the formation of isomeric dihydrofuro[2,3-*d*]pyrimidine compound **5a**. The study of the NOESY NMR spectra confirmed the formation of the *cis* form of the compound **5a** as the two protons showed strong correlation in the spectra. The formation of these *cis* and *trans* forms of regioisomeric compounds are in contrary to many other reactions which produced exclusively one regioisomer of the fused dihydrofuran derivatives, and usually the *trans* form with coupling constants in the range of J = 4-6 Hz.[18] In our present case, it might be because of the unique nonplanner structure of the substituted uracil moiety. In IR spectrum, stretching frequencies at 1687.2, 1557.6 cm^{-1} of **4a** and 1685.4, 1560.2 cm^{-1} of **5a** confirmed the presence of the furan ring and amide C=O functional groups in both the compounds. The mass spectrum shows, a sharp distinguishable peak of compound **4a** and **5a** at 363.41 $[M+H]^+$ and 363.32 $[M+H]^+$ respectively. Interestingly, even though we considered the formation of the compound **5** as unexpected, a literature survey revealed one example which reported the formation of exclusively this type of isomeric compounds (two compounds only) by using sulfur ylides, and our product **5h** was found to be comparable in all respect to one of that compounds.[17] Again, although the compound **4a** was the usual expected product from the reaction of nitrogen ylides, the formation of the unexpected product **5a** in a comparable ratio might be because of the typical nonplanner structure of pyrimidinedione moiety.

Then we studied the effect of substituent of the substrates in the reaction process. It was observed that the reaction requires 2-6 h in refluxing conditions depending upon the substituent on aryl aldehyde and pyridinium ylide to afford the desired compounds. Since aromatic aldehydes are more reactive than aliphatic towards nucleophillic attack, hence more emphasis was given on aryl aldehyde. The reactions were smooth and easy in aldehydes having electron withdrawing substituent (NO_2, Cl, Br) in comparison to electron releasing substituent (H, CH_3) and also provide better yield of the products in less reaction time.

Mechanism for the formation of dihydrofuro[2,3-*d*]-pyrimidines 4a and 5a



Scheme 2

To expand the scope of the reaction, different pyridinium ylides were generated from various pyridinium salts *viz.* phenacyl pyridinium bromide, 1-ethoxy carbonyl methyl pyridinium iodide[19] and 1-cyanomethyl pyridinium bromide,[20] and utilized during the course of the study. Benzylpyridinium ylide obtained from benzylpyridinium bromide was most effective which may be accounted from the mechanism that interprets the resonance stabilization of enolate ion by phenyl

group. The reaction with 1-cyanomethyl pyridinium ylide was not smooth, and provided less yields even on increasing the reaction time, hence we have limited our experiment with this ylide.

The effect of substituents in barbituric acids was also studied properly and observed that *N*,*N*-dimethylbarbituric acid was more reactive than *N*-methylbarbituric acid and products were obtained in better yield in less reaction time. Moreover, in case of *N*-methylbarbituric acid, selectively the more favoured *N*-methyl amidic carbonyl group involved in the cyclization process to produce only the two regioisomeric dihydrofuro[2,3-*d*]pyrimidines (Entry 6 & 13, Table 2) as expected, and such selectivity is well precedented.[21]

A reasonable mechanism for the formation of the regioisomers is depicted in the scheme **2** taking the formation of **4a** and **5a** as example. The reaction occurred *via* initial formation of the knoevenagel condensed product **[A]** from the reaction of *N*,*N*-dimethylbarbituric acid **1** (R^1 = Me) and benzaldehyde **2** (Ar = Ph), and the ylide **[B]** from the benzylpyridinium bromide **3** (R^2 = COPh) in the presence of triethyl amine (Scheme 2). The intermediates **[A]** and **[B]** then reacted to produce the intermediate **[C]** which followed two different reaction path to afford the product **4a** & **5a** respectively. In path I, the intermediate **[C]** produced the compound **4a** by a direct cyclization process by eliminating pyridine. But in path II, first, intermediate **[D]** with the cyclopropane ring was formed, which underwent an intramolecular ring transformation, and proceeded through the intermediates **[E]** and **[F]** in the presence of base to produce the product **5a**. The mechanism for the formation of both types of compounds from ylides is well documented.[13c,17]

In conclusion, we have reported an unprecedented regioisomeric synthesis of some highly functionalized dihydrofuro[2,3-*d*]pyrimidines by generating nitrogen ylides in an one-pot three-components reaction barbituric acids, aryl aldehydes and pyridinium bromides in the presence of triethylamine as base. The products were formed in a diastereoselective manner and overall good yields. A suitable mechanism is given for the reaction process which shows that nitrogen ylides involve in [4+1] annulations as well as [2+1] annulation followed by intramolecular ring transformation in the presence of base to afford two isomeric products.

4. Experimental Section

All chemicals were purchased from Merck and Aldrich chemical companies. The reagents and solvents were used without drying. The IR spectra were recorded on Perkin Elmer system 2000 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR Spectra were recorded on Bruker AV500 Avance – III 500 MHz and 125 MHz FT NMR in $CDCl_3$ using TMS as an internal standard. Chemical shifts (δ units) are given from TMS (0 ppm). Chemical shifts for $CDCl_3$ were reported at 7.26 ppm (δ units). Mass spectra were recorded in Bruker Daltonics ESQUIRE 3000 LC ESI ion trap mass spectrometer. Analytical thin layer chromatography (TLC) was performed using E-Merck aluminium-backed silica gel plates coated with 0.2 mm thickness of silica gel. Melting points (uncorrected) were determined in open capillary tubes on a Buchi B-540 apparatus. Elemental analyses were performed on Perkin-Elmer 2400 spectrometer at the Analytical Chemistry Division, CSIR-NEIST, Jorhat.

General Procedure for preparation of dihydrofuro[2,3-*d*]pyrimidines 4 & 5: A mixture of *N*,*N*-dimethylbarbituric acid **1** (R^1 = Me, 156 mg, 1mmol), benzaldehyde **2** (Ar = Ph, 106 mg, 1mmol) and benzylpyridinium **3** (R^2 = COPh, 278 mg, 1mmol) in acetonitrile (5 mL) were taken in round bottom flask. Triethyl amine (121 mg, 1.20 mmol) were added to the reaction mixture and allowed to reflux for 4 h at 80 ˚C. The solvent was removed under reduced pressure, and the crude products were purified by column chromatography (silica gel 100-200#, petroleum ether/ethyl acetate, 9:1 ratio), which afforded the desired dihydrofuro[2,3-*d*]pyrimidine derivatives **4a** and **5a** in 40% (144 mg) and 38% (137 mg) respectively.

Similarly, compounds **4b-o** and **5b-o** were synthesized and characterized.

6-Benzoyl-1,3-dimethyl-5-phenyl-5,6-dihydrofuro[2,3-d]-pyrimidine-2,4(1H,3H)-dione ***(4a)***: Yield: 144 mg (40%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.50; mp. 134.0-135.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.22 (s, 3H), 3.24 (s, 3H), 4.17 (d, *J* = 9.5 Hz, 1H), 4.26 (d, *J* = 9.5 Hz, 1H), 7.24-8.24 (m, 10H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.8, 29.0, 47.9, 87.4, 90.6, 128.1 (2C), 128.3 (2C), 128.6 (2C), 128.8, 129.5 (2C), 131.0, 133.7, 136.0, 151.3, 163.4, 165.7, 191.2; IR (KBr, cm^{-1}) ν_{max}:1180.7, 1451.9, 1679.1, 2960.4; MS (ESI): 363.4 $[M+H]^+$; Anal. Cald. For $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73%. Found: C, 69.72; H, 5.02; N, 7.75%.

5-Benzoyl-1,3-dimethyl-6-phenyl-5,6-dihydrofuro-[2,3-d]-pyrimidine-2,4(1H,3H)-dione ***(5a)***: Yield: 137 mg (38%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.32; mp. 131.0.-132.1 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.19 (s, 3H), 3.32 (s, 3H), 5.16 (d, *J* = 5.5 Hz, 1H), 6.04 (d, *J* = 5.5 Hz, 1H), 7.18-8.02 (m, 10H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.9, 29.2, 53.9, 87.4, 89.7, 125.6 (2C), 128.9 (2C), 129.2 (2C), 129.2 (2C), 129.6, 133.1, 133.9, 135.7, 149.4, 159.4, 162.2, 191.5; IR (KBr, cm^{-1}) ν_{max}:1180.5, 1451.4, 1678.3, 2960.2; MS (ESI): 363.3 $[M+H]^+$; Anal. Cald. For $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73%. Found: C, 69.55; H, 5.03; N, 7.74%.

6-Benzoyl-1,3-dimethyl-5-(p-tolyl)-5,6-dihydrofuro-[2,3-d-]pyrimidine-2,4(1H,3H)-dione ***(4b)***: Yield: 135 mg (36%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.52; mp. 131.1.-133.6 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.17 (s, 3H), 3.21 (s, 3H), 3.24 (s, 3H), 4.03 (d, *J* = 9.5 Hz, 1H), 4.20 (d, *J* = 9.5 Hz, 1H), 7.21-7.64 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.1, 28.8, 28.9, 46.7, 86.3, 90.1, 122.9, 128.1 (2C), 128.8 (2C),130.1, 131.1 (2C), 131.5 (2C), 133.8, 135.8, 151.1, 163.3, 165.4, 190.7; IR (KBr, cm^{-1}) ν_{max}: 1180.9, 1452.2, 1678.8, 2960.5; MS (ESI): 377.1 $[M+H]^+$; Anal. Cald. For $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44%. Found: C, 70.32; H, 5.37; N, 7.42%.

5-Benzoyl-1,3-dimethyl-6-(p-tolyl)-5,6-dihydrofuro-[2,3-d]-pyrimidine-2,4(1H,3H)-dione ***(5b)*****:** Yield: 124 mg (33%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.33; mp. 130.2.-130.9 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.17 (s, 3H), 3.20 (s, 3H), 3.25 (s, 3H), 4.95 (d, *J* = 6 Hz, 1H), 5.82 (d, *J* = 6 Hz, 1H), 7.18-7.62 (m, 9H); ^{13}C NMR ($CDCl_3$, 125

MHz) δ 21.1, 28.7, 28.8, 45.6, 87.2, 90.3, 123.4, 128.2 (2C), 129.3 (2C),130.4, 131.0 (2C), 131.7 (2C), 133.8, 136.2, 150.4, 164.1, 165.2, 191.2; IR (KBr, cm^{-1}) ν_{max}: 1181.6, 1451.8, 1678.7, 2960.9; MS (EI): 377.3 $[M+H]^+$; Anal. Cald. For $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44%. Found: C, 70.18; H, 5.34; N, 7.45%.

6-Benzoyl-1,3-dimethyl-5-(p-nitro-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(4c)***: Yield: 183.2 mg (45%); Orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.47; mp. 151.5-153.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.20 (s, 3H), 3.22 (s, 3H), 4.15 (d, *J* = 9.5 Hz, 1H), 4.25 (d, *J* = 9.5 Hz, 1H), 7.22-8.28 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.0, 29.2, 41.1, 87.4, 90.3, 123.5 (2C), 127.9 (2C), 128.9 (2C), 130.5 (2C), 134.0, 135.6, 138.6, 147.8, 150.9, 163.3, 164.9, 190.1; IR (KBr, cm^{-1}) ν_{max}: 1180.6, 1451.4, 1678.1, 2960.3; MS (ESI): 408.3 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}N_3O_6$: C, 61.91; H, 4.21; N, 10.31%. Found: C, 62.00; H, 4.22; N, 10.29%.

5-Benzoyl-1,3-dimethyl-6-(p-nitro-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(5c)***: Yield: 171 mg (42%); Orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.29; mp. 149.2-150.9 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.24 (s, 3H), 3.35 (s, 3H), 5.01 (d, *J* = 6 Hz, 1H), 6.01 (d, *J* = 6 Hz, 1H), 7.03-8.20 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.9, 29.5, 53.0, 80.3, 85.8, 123.5 (2C), 128.0 (2C), 128.9 (2C), 130.5 (2C), 133.9, 135.7, 138.6, 147.8, 151.5, 162.9, 164.9, 190.0; IR (KBr, cm^{-1}) ν_{max}: 1180.7, 1451.3, 1678.0, 2960.2; MS (ESI): 408.5 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}N_3O_6$: C, 61.91; H, 4.21; N, 10.31%. Found: C, 61.90; H, 4.20; N, 10.32%.

6-Benzoyl-1,3-dimethyl-5-(p-chloro-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(4d)***: Yield: 170.3 mg (43%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.48; mp. 146.7-148.9 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.14 (s, 3H), 3.18 (s, 3H), 3.98 (d, *J* = 9.5 Hz, 1H), 4.15 (d, *J* = 9.5 Hz, 1H), 7.09-7.85 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.8, 28.9, 41.4, 86.7, 90.2, 128.1 (2C), 128.6 (2C), 128.8 (2C), 129.3. 131.2 (2C), 133.8, 134.6, 135.8, 151.2, 163.3, 165.4, 190.7; IR (KBr, cm^{-1}) ν_{max}: 1181.0, 1451.8, 1680.1, 2960.7; MS (ESI): 397.1 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}ClN_2O_4$: C, 63.56; H, 4.32; N, 7.06%. Found: C, 63.71; H, 4.31; N, 7.07%.

5-Benzoyl-1,3-dimethyl-6-(p-chloro-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(5d)***: Yield: 158 mg (40%); Light Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.31; mp. 139.9-142.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.27 (s, 3H), 3.41 (s, 3H), 5.18 (d, *J* = 5.5 Hz, 1H), 6.11 (d, *J* = 5.5 Hz, 1H), 7.21-7.62 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.0, 29.7, 53.8, 87.3, 89.8, 127.2 (2C), 128.7 (2C), 129.3 (2C), 129.4 (2C), 134.1, 135.6, 135.6, 136.3, 151.3, 159.3, 162.0, 197.8 ; IR (KBr, cm^{-1}) ν_{max}: 1180.5, 1450.7, 1679.8, 2960.5; MS (ESI): 397.3 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}ClN_2O_4$: C, 63.56; H, 4.32; N, 7.06%. Found: C, 63.78; H, 4.33; N, 7.05%.

6-Benzoyl-1,3-dimethyl-5-(p-bromo-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(4e)***: Yield: 185 mg (42%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.48; mp. 143.1-144.5 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.12 (s, 3H), 3.16 (s, 3H), 3.94 (d, *J* = 10.5 Hz, 1H), 4.15 (d, *J* = 10.5 Hz, 1H), 7.12-7.89 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.8, 28.9, 46.7, 87.3, 89.8, 122.9, 128.1 (2C), 128.8 (2C), 130.1, 131.1 (2C), 131.5 (2C), 133.8, 135.8, 151.2, 163.3, 165.4, 190.8; IR (KBr, cm^{-1}) ν_{max}: 1180.4, 1451.9, 1678.9, 2960.7; MS (ESI): 442.2 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}BrN_2O_4$: C, 57.16; H, 3.88; N, 6.35%. Found: C, 57.35; H, 3.89; N, 6.33%.

5-Benzoyl-1,3-dimethyl-6-(p-bromo-phenyl)-5,6-dihydrofuro-[2,3-d]pyrimidine-2,4(1H,3H)-dione ***(5e)***: Yield: 176 mg (40%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.32; mp. 137.2-138.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.12 (s, 3H), 3.28 (s, 3H), 4.72 (d, *J* = 6 Hz, 1H), 5.97 (d, *J* = 6 Hz, 1H), 7.08-7.88 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.5, 29.7, 53.7, 87.2, 89.7, 123.6, 127.4 (2C), 128.3 (2C), 128.7 (2C), 132.5 (2C), 134.2, 135.7, 136.9, 151.3, 159.4, 162.2, 197.7; IR (KBr, cm^{-1}) ν_{max}: 1180.2, 1452.0, 1678.4, 2960.8 ; MS (ESI): 442.5 $[M+H]^+$; Anal. Cald. For $C_{21}H_{17}BrN_2O_4$: C, 57.16; H, 3.88; N, 6.35%. Found: C, 57.25; H, 3.87; N, 6.36%.

6-Benzoyl-3-methyl-5-phenyl-5,6-dihydrofuro[2,3-d]-pyrimidine-2,4(1H,3H)-dione ***(4f)***: Yield: 122 mg (35%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.49; mp.137.5-138.1 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.13 (s, 3H), 4.03 (d, *J* = 9.5 Hz, 1H), 4.17 (d, *J* = 9.5 Hz, 1H), 7.12-7.90 (m, 10H), 10.33 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.7, 47.8, 87.2, 91.4, 128.3 (2C), 128.6 (2C), 129.1, 129.4 (2C), 129.6 (2C), 131.1, 133.4, 134.0, 152.4, 162.3, 165.8, 190.3; IR (KBr, cm^{-1}) ν_{max}: 1191.0, 1681.2, 1744.3, 2924.9; MS (ESI): 349.4 $[M+H]^+$; Anal. Cald. For $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04%. Found: C, 68.92; H, 4.64; N, 8.05%.

5-Benzoyl-3-methyl-6-phenyl-5,6-dihydrofuro[2,3-d]-pyrimidine-2,4(1H,3H)-dione ***(5f)*** : Yield: 112 mg (32%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.30; mp. 135.2-135.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.18 (s, 3H), 5.19 (d, *J* = 5.5 Hz, 1H), 6.03 (d, *J* = 5.5 Hz, 1H), 7.15-8.01 (m, 10H), 10.21 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.8, 55.4, 87.3, 89.8, 125.6 (2C), 128.8 (2C), 129.0 (2C), 129.2 (2C), 129.7, 133.2, 133.9, 135.6, 149.5, 158.3, 162.3, 191.3; IR (KBr, cm^{-1}) ν_{max}:1191.6, 1680.8, 1743.6, 2925.5; MS (ESI): 349.3 $[M+H]^+$; Anal. Cald. For $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04%. Found: C, 68.99; H, 4.62; N, 8.03%.

Ethyl-1,3-dimethyl-2,4-dioxo-5-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4g)***: Yield: 132 mg (40%); Dark yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.49; mp. 182.5-183.9 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.25 (t, 3H), 3.25 (s, 3H), 3.32 (s, 3H), 4.04 (d, *J* = 9.5 Hz, 1H), 4.18-4.25 (m, 3H), 7.18-7.47 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 28.0, 29.4, 52.5, 62.0, 88.7, 90.0, 125.6 (2C), 126.7, 128.7 (2C), 137.4, 151.4, 159.2, 161.9, 171.1; IR (KBr, cm^{-1}) ν_{max}: 1192.0, 1681.3, 1734.9, 2925.0; MS (ESI): 331.2 $[M+H]^+$; Anal. Cald. For $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48%. Found: C, 61.59; H, 5.50; N, 8.45%.

Ethyl-1,3-dimethyl-2,4-dioxo-6-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carboxylate ***(5g)***: Yield:

119.1 mg (36%); Dark yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.26; mp. 178.7-179.2 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.18 (t, 3H), 3.21 (s, 3H), 3.32 (s, 3H), 4.15-4.22 (m, 3H), 5.96 (d, *J* = 6 Hz, 1H), 7.18-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 28.3, 29.5, 52.5, 62.0, 85.9, 90.0, 125.5 (2C), 128.5 (2C), 129.0, 137.5, 151.4, 159.3, 161.8, 171.4; IR (KBr, cm^{-1}) ν_{max}: 1191.4, 1681.1, 1735.2, 2925.2; MS (ESI): 331.4 $[M+H]^+$; Anal. Cald. For $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48%. Found: C, 61.93; H, 5.47; N, 8.50%.

Ethyl-5-(p-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro-[2,3-d]pyrimidine-6-carboxylate ***(4h)***: Yield: 115 mg (32%); Colourless solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.50; mp. 173.4-175.2 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.97 (t, 3H), 3.13 (s, 3H), 3.27 (s, 3H), 3.79(s, 3H,OMe), 3.94(d, *J* = 9.5 Hz, 1H), 4.08 (d, *J* = 9.5 Hz, 1H), 4.38 (m, 2H), 6.84-7.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 28.5, 29.6, 52.5, 60.2, 62.4, 87.7, 89.2, 123.6, 127.2 (2C), 132.0(2C), 151.4, 159.2, 161.8, 16,1.9 169.4; IR (KBr, cm^{-1}) ν_{max}: 1190.1, 1683.1, 1734.0, 2923.7; MS (ESI): 361.2 $[M+H]^+$; Anal. Cald. For $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77%. Found: C, 59.97; H, 5.58; N, 7.75%.

Ethyl-6-(p-methoxyphenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro-[2,3-d]pyrimidine-5-carboxylate ***(5h)***: Yield: 101 mg (28%); Colourless solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.28; mp. 170.1-172.3˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.24 (t, 3H), 3.26 (s, 3H), 3.33 (s, 3H), 3.76 (s, 3H, OMe), 4.16-4.26 (m,3H), 5.98 (d, *J* = 6 Hz, 1H), 7.19-7.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 28.0, 29.5, 52.4, 56.0, 61.9, 86.0, 90.3, 114.2, 127.8 (2C),129.5 (2C), 151.4, 159.2, 161.7, 161.9, 171.5; IR (KBr, cm^{-1}) ν_{max}: 1190.7, 1684.1, 1733.7, 2924.5; MS (ESI): 361.1 $[M+H]^+$; Anal. Cald. For $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77%. Found: C, 60.01; H, 5.60; N, 7.79%.

Ethyl-1,3-dimethyl-2,4-dioxo-5-(p-tolyl)-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4i)***: Yield: 123 mg (36%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.51; mp. 175.4-177.6 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.19 (t, 3H), 2.24 (s, 3H), 3.08 (s, 3H), 3.11 (s, 3H), 3.67 (d, *J* = 9.5 Hz, 1H), 3.84 (d, *J* = 9.5 Hz, 1H), 4.19 (m, 2H),7.01-7.23 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 20.9, 28.8, 29.5, 46.0, 62.2, 86.0, 88.2, 126.6 (2C), 129.3 (2C), 134.4, 139.6, 151.5, 161.9, 162.8, 171.5; IR (KBr, cm^{-1}) ν_{max}: 1190.9, 1680.1, 1735.1, 2925.5; MS (ESI): 345.5 $[M+H]^+$; Anal. Cald. For $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13%. Found: C, 63.00; H, 5.87; N, 8.10%.

Ethyl-1,3-dimethyl-2,4-dioxo-6-(p-tolyl)-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carboxylate ***(5i)***: Yield: 116 mg (34%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.28; mp. 169.9-172.4 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.23 (t, 3H), 2.32 (s, 3H), 3.30 (s, 3H), 3.39 (s, 3H), 4.22-4.30 (m, 3H), 5.99 (d, *J* = 6 Hz, 1H),6.84-7.38 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 21.1, 28.0, 29.2, 52.4, 61.9, 86.0, 88.9, 125.8 (2C), 128.9, 129.6 (2C), 139.6, 151.4, 159.2, 161.7, 169.6; IR (KBr, cm^{-1}) ν_{max}: 1190.8, 1680.0, 1734.8, 2925.6; MS (ESI): 345.1 $[M+H]^+$; Anal. Cald. For $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13%. Found: C, 62.93; H, 5.86; N, 8.15%.

Ethyl-1,3-dimethyl-5-(p-nitrophenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4j)***: Yield: 165 mg (44%); Dark orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.44; mp. 204.3- 207.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.21 (t, 3H), 3.13 (s, 3H), 3.31 (s, 3H), 3.65 (d, *J* = 9.5 Hz, 1H), 3.91 (d, *J* = 9.5 Hz, 1H), 4.22 (m, 2H), 7.38 (d, *J* = 11.5 Hz, 2H), 8.11 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 28.8, 28.9, 44.6, 62.1, 87.1, 89.1, 123.4 (2C), 124.2, 130.4 (2C), 138.5, 147.7, 150.9, 163.2, 165.4; IR (KBr, cm^{-1}) ν_{max}: 1191.2, 1515.5, 1734.0, 2925.9; MS (ESI): 376.3 $[M+H]^+$; Anal. Cald. For $C_{17}H_{17}N_3O_7$: C, 54.40; H, 4.57; N, 11.20%. Found: C, 54.59; H, 4.58; N, 11.18%.

Ethyl-1,3-dimethyl-6-(p-nitrophenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carboxylate ***(5j)***: Yield: 150 mg (40%); Orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.22; mp. 200.9-202.1 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.41 (t, 3H), 3.21 (s, 3H), 3.40 (s, 3H), 4.09 (d, *J* = 6 Hz, 1H), 4.45 (m, 2H), 6.00 (d, *J* = 6 Hz, 1H), 7.20-8.20 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 28.9, 29.0, 52.3, 62.2, 88.2, 89.0, 123.3 (2C), 125.3, 130.5 (2C), 138.4, 147.6, 151.0, 163.1, 166.3; IR (KBr, cm^{-1}) ν_{max}: 1191.1, 1515.4, 1680.3, 1734.1, 2925.8 ; MS (ESI): 376.6 $[M+H]^+$; Anal. Cald. For $C_{17}H_{17}N_3O_7$: C, 54.40; H, 4.57; N, 11.20%. Found: C, 54.49; H, 4.55; N, 11.17%.

Ethyl-1,3-dimethyl-5-(p-chlorophenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4k)***: Yield: 153 mg (42%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.46; mp. 198.1- 199.5 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.21 (t, 3H), 3.13 (s, 3H), 3.28 (s, 3H), 3.63 (d, *J* = 9.5 Hz, 1H), 3.81 (d, *J* = 9.5 Hz, 1H), 4.20 (m, 2H), 7.09-7.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 28.8, 28.8, 46.2, 61.9, 87.4, 89.9, 128.4 (2C), 129.3, 130.7 (2C), 134.5, 151.2, 163.1, 165.8, 165.9; IR (KBr, cm^{-1}) ν_{max}: 1192.5, 1680.7, 1735.1, 2925.4; MS (ESI): 365.3 $[M+H]^+$; Anal. Cald. For $C_{17}H_{17}ClN_2O_5$: C, 55.97; H, 4.70; N, 7.68%. Found: C, 56.08; H, 4.69; N, 7.71%.

Ethyl-1,3-dimethyl-6-(p-chlorophenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carboxylate ***(5k)***: Yield: 142.1 mg (39%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.23; mp. 195.7-197.4 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.29 (t, 3H), 3.25 (s, 3H), 3.30 (s, 3H), 4.10 (d, *J* = 6 Hz, 1H), 4.20 (m, 2H), 5.93 (d, *J* = 6 Hz, 1H), 7.13-7.34 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 29.3, 29.7, 52.7, 62.2, 85.9, 88.4, 127.1 (2C), 128.3, 129.2 (2C), 130.6, 151.4, 159.2, 161.9, 171.3; IR (KBr, cm^{-1}) ν_{max}: 1191.3, 1680.5, 1734.9, 2925.8; MS (ESI): 365.1 $[M+H]^+$; Anal. Cald. For $C_{17}H_{17}ClN_2O_5$: C, 55.97; H, 4.70; N, 7.68%. Found: C, 56.10; H, 4.71; N, 7.70%.

Ehyl-1,3-dimethyl-5-(p-bromophenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4l)***: Yield: 167 mg (41%); Light orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.46; mp. 193.2-194.6.2 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.28 (t, 3H), 3.13 (s, 3H), 3.32 (s, 3H), 3.62 (d, *J* = 9.5 Hz, 1H), 3.79 (d, *J* = 9.5 Hz, 1H), 4.20 (m, 2H), 7.05-7.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 28.8, 29.5, 46.1, 61.9, 85.0, 86.8, 122.7, 130.0, 131.0 (2C), 131.4 (2C), 151.2, 163.1, 165.7, 165.8; IR (KBr, cm^{-1}) ν_{max}: 1190.8, 1681.1, 1734.7, 2925.6; MS (ESI): 410.1 $[M+H]^+$; Anal. Cald.

For $C_{17}H_{17}BrN_2O_5$: C, 49.89; H, 4.19; N, 6.85%. Found: C, 50.03; H, 4.20; N, 6.83%.

Ethyl-1,3-dimethyl-6-(p-bromo-phenyl)-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro-[2,3-d]pyrimidine-5-carboxylate ***(5l)***: Yield: 143 mg (35%); Light orange solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.24; mp. 190.7-192.3 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.32 (t, 3H), 3.32 (s, 3H), 3.39 (s, 3H), 4.17 (d, *J* = 6 Hz, 1H), 4.30 (m, 2H), 5.98 (d, *J* = 6 Hz, 1H), 7.14-7.61 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 28.5, 29.5, 52.5, 62.4, 85.7, 87.7, 123.6, 127.2 (2C), 132.0 (2C), 136.4, 151.3, 159.1, 161.8, 171.0; IR (KBr, cm^{-1}) ν_{max}: 1191.7, 1681.2, 1734.1, 2925.8 ; MS (ESI): 410.3 $[M+H]^+$; Anal. Cald. For $C_{17}H_{17}BrN_2O_5$: C, 49.89; H, 4.19; N, 6.85%. Found: C, 50.05; H, 4.20; N, 6.86%.

Ethyl-3-methyl-2,4-dioxo-5-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carboxylate ***(4m)***: Yield: 105 mg (33%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.47; mp. 186.6-188.40 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.24 (t, 3H), 3.25 (s, 3H), 4.01 (d, *J* = 9.5 Hz, 1H), 4.15-4.22 (m, 3H), 7.15-7.37 (m, 5H), 10.31 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 28.0, 53.2, 62.1, 88.8, 91.2, 125.6 (2C), 126.8, 128.6 (2C), 137.5, 151.3, 158.3, 162.9, 172.3; IR (KBr, cm^{-1}) ν_{max}:1191.2, 1680.5, 1743.4, 2925.3; MS (ESI): 317.3 $[M+H]^+$; Anal. Cald. For $C_{16}H_{16}N_2O_5$: C, 60.75; H, 5.10; N, 8.86%. Found: C, 60.79; H, 5.09; N, 8.85%.

Ethyl-3-methyl-2,4-dioxo-6-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carboxylate ***(5m)***: Yield: 95.35 mg (30%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.25; mp. 185.1-186.7 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.17 (t, 3H), 3.22 (s, 3H), 4.14-4.26 (m, 3H), 5.92 (d, *J* = 6 Hz, 1H), 7.17-7.36 (m, 5H), 10.33 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 28.5, 53.6, 62.1, 86.9, 90.0, 125.6 (2C), 128.4 (2C), 129.1, 137.6, 151.3, 159.4, 162.3, 172.3; IR (KBr, cm^{-1}) ν_{max}:1191.4, 1680.9, 1743,0, 2925.1; MS (ESI): 317.5 $[M+H]^+$; Anal. Cald. For $C_{16}H_{16}N_2O_5$: C, 60.75; H, 5.10; N, 8.86%. Found: C, 60.77; H, 5.11; N, 8.87%.

1,3-Dimethyl-2,4-dioxo-5-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carbonitrile ***(4n)***: Yield: 105 mg (37%); Dark yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.44; mp. 96.4-96.8 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.20 (s, 3H), 3.48 (s, 3H), 4.21 (d, *J* = 9 Hz, 1H), 5.30 (d, *J* = 9 Hz, 1H), 7.12-7.51 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.0, 29.2, 45.1, 80.1, 88.5, 114.0, 123.4, 128.1, 130.6 (2C), 131.8 (2C), 150.5, 162.0, 163.8; IR (KBr, cm^{-1}) ν_{max}: 1194.4, 1681.2, 2251.5, 2925.4; MS (ESI): 284.5 $[M+H]^+$; Anal. Cald. For $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.63; N, 14.83%. Found: C, 63.79; H, 4.64; N, 14.85%.

1,3-Dimethyl-2,4-dioxo-6-phenyl-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carbonitrile ***(5n)*****:** Yield: 96 mg (34%); Yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.20; mp. 94.2-95.1 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.19 (s, 3H), 3.27 (s, 3H), 4.82 (d, *J* = 6 Hz, 1H), 4.94 (d, *J* = 6 Hz, 1H), 7.10-7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.1, 29.3, 39.0, 80.1, 87.5, 115.1, 123.3, 128.1, 130.5 (2C), 131.8 (2C), 150.6, 162.1, 164.7; IR (KBr, cm^{-1}) ν_{max}: 1194.3, 1681.5, 2251.4, 2925.3; MS (ESI): 284.1 $[M+H]^+$; Anal. Cald. For $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.63; N, 14.83%. Found: C, 63.58; H, 4.62; N, 14.82%.

5-(p-Chlorophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-6-carbonitrile ***(4o)***: Yield: 120.2 mg (38%); Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.42; mp. 100.7-101.2 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.28 (s, 3H), 3.35 (s, 3H), 4.29 (d, *J* = 9.5 Hz, 1H), 5.60 (d, *J* = 9.5 Hz, 1H), 7.15-7.55 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 28.1, 29.5, 45.1, 80.1, 87.0, 119.5, 128.0 (2C), 129.8 (2C), 134.0, 139.5, 151.0, 160.1, 161.7; IR (KBr, cm^{-1}) ν_{max}: 1681.8, 2251.3, 2925.7, 1194.3; MS (ESI): 318.2 $[M+H]^+$; Anal. Cald. For $C_{15}H_{12}ClN_3O_3$: C, 56.70; H, 3.81; N, 13.23%. Found: C, 56.73; H, 3.82; N, 13.25%.

6-(p-Chlorophenyl)-1,3-dimethyl-2,4-dioxo-1,2,3,4,5,6-hexahydrofuro[2,3-d]pyrimidine-5-carbonitrile ***(5o)***: Yield: 111 mg (35%);Light yellow solid; Rf (Pet. Ether. 60-80/EtOAc, 8:2) 0.18; mp. 98.2-99.5 ˚C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.20 (s, 3H), 3.24 (s, 3H), 4.79 (d, *J* = 6 Hz, 1H)), 4.93 (d, *J* = 6 Hz, 1H), 7.09-7.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 29.5, 29.7, 38.1, 82.4, 88.8, 116.6, 126.8 (2C), 129.7 (2C), 134.1, 136.5, 150.9, 158.3, 161.8; IR (KBr, cm^{-1}) ν_{max}: 2253.1, 1680.2, 1194.6, 2925.3; MS (ESI): 318.5 $[M+H]^{+-}$ Anal. Cald. For $C_{15}H_{12}ClN_3O_3$: C, 56.70; H, 3.81; N, 13.23%. Found: C, 56.84; H, 3.79; N, 13.27%.

Acknowledgements

We thank DST, New Delhi and CSIR, New Delhi for financial assistance (CAAF-NE Project).

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